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REMARKS

Upon entry of the amendments herein, claims 1, 2, 27-34 and 36-39 remain pending in the application. Claims 1 and 2 have been amended herein. Claims 29, 31, 34, and 36-39 currently stand withdrawn from consideration pending their being rejoined to the other pending claims upon determination of allowable subject matter.

Claim 27 has been rejected as being indefinite for reciting that substituent R<sub>6</sub> is optionally substituted; the Examiner asserts that there is insufficient antecedent basis for this limitation. The Examiner further clarifies his stance by stating that "[C]laim 1 from which claim 27 depends does not have basis for, e.g. R<sub>6</sub> = oxo substituted on aryl. Neither is there support for other groups such as acyl, acylamino, amino cyano, thio, nitro, aroyl etc." This assessment is in error; there is support for all of the substitutions enumerated by the Examiner, as well as the other substitutions recited in the claims.

Applicants wish to point out in the first place that in the Office Action mailed March 22, 2007 in application Serial No. 11/293,060, a divisional of the present application, the Examiner (tacitly) acknowledged that substituent R<sub>6</sub> can be substituted, even though such is not expressly stated in claim

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1. More particularly, in leveling a prior art rejection in the divisional (over U.S. Patent No. 4,560,680 to Ryono et al.), the Examiner cited an instance wherein substituent  $R_6$  according to the instant invention is substituted, specifically, wherein  $R_6$  is  $(CH_2)_4$ -phenyl. This citation was used as a basis for making the assertion that certain compounds of the present invention are anticipated by the Ryono reference. Thus, in the present application, the Examiner is contradicting his stance in the divisional application.

Even more telling, it must further be noted that the Examiner raised essentially the same issues in the November 4, 2005 Office Action in the present application. Although the issues were raised in the November 4, 2005 Action in connection with 35 U.S.C. §112, first paragraph and the written description requirement, while the issues in the present application have been raised under U.S.C. §112, second paragraph, in connection with indefiniteness, the basic issue is the same. That issue is whether or not there is support in the application for  $R_6$  being substituted. As previously set forth by Applicants and as previously accepted by the Examiner, there is indeed sufficient support. Applicants wish to remind the Examiner that the arguments they provided in their May 2, 2006 response to the written description issues raised in the present application

were found persuasive, the Examiner acknowledging that there is support for substitution on, in particular,  $R_6$ .

Thus, the Examiner has already acknowledged, both in the divisional application and in the present application, that there is support for the idea that substituent  $R_6$  can be substituted. The Examiner is now attempting to resurrect issues that were fully and persuasively addressed earlier during prosecution of the present application. In the interest of completeness, Applicants have reproduced below for the Examiner's convenience the arguments most pertinent to the present rejections and which arguments were found persuasive in Applicants' earlier response.

While it may be true that claim 1 does not literally recite that  $R_6$  is optionally substituted, focusing on this situation does not appropriately take into account the teaching of the present application. Page 11, lines 1-7; page 12, lines 6-10; and page 12, lines 14-16 provide further teaching as to what is meant by the " $C_1$ - $C_6$  alkyl," "aryl" and "cycloalkyl" groups in the definition of substituent  $R_6$  in claim 1. In each instance, it is taught that the groups can be, inter alia, "substituted or unsubstituted." Lines 6-11 of page 13 teach what is meant by "substituted" in connection with the  $C_1$ - $C_6$  alkyl, cycloalkyl and aryl groups, as well as the  $H_2N-CH(Z)-CONH-CH(Z)-$  and the  $H_2N-$

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CH(2)-groups that make up the remainder of the definition of substituent  $R_6$  currently found in claim 1.

Accordingly, it is clear from the disclosure in the specification that (whether it is expressly stated in the claims or not)  $R_6$  can be substituted or unsubstituted, and claim 1 must be interpreted as encompassing both possibilities. Thus, it must be held that claim 1 provides sufficient antecedent basis for the language " $R_6$  is optionally substituted..." in claim 27. It is widely accepted in U.S. patent practice that literal antecedent basis is not by any means required in all instances. Claim 27 must be viewed as serving merely to specifically identify ways in which the groups recited in claim 1 in the definition of  $R_6$  can be substituted, when they are substituted.

The idea that the Examiner previously considered Applicants' arguments and the support in the specification pointed out by Applicants, and considered them persuasive, is further reinforced by the fact that these issues were not raised during consideration of claims 18 and 19 in the copending divisional application, Serial No. 11/293,060. That is to say that such issues were not brought to bear in the recent (March 22, 2007) Office Action in the divisional. Claims 18 and 19 in the divisional are the respective counterparts to claims 27 and 28 in the instant application.

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It is also important to note that Examples 1-4, 17 and 18 of the instant specification require that R<sub>6</sub> be substituted and thus provide firm and ample support for what was originally intended as the scope of the claimed genus of compounds.

For all the reasons repeated above in addressing the same basic issue raised in an earlier Office Action, albeit now raised in the guise of a rejection under a different part of the statute, it must be held that claim 1 provides sufficient antecedent basis for the language of claim 27 cited by the Examiner and that claim 27 thus meets the requirements of 35 U.S.C. §112, second paragraph.

Claims 27-30 and 32 have been objected to as not complying with 35 C.F.R. §1.75(c). There is no basis for this objection, and it must be withdrawn.

In the first place, contrary to the Examiner's assertion, there is nothing in either 37 C.F.R. §1.75(c) or in MPEP §608.01(n), also cited by the Examiner, that indicates that "a multiple dependent claim may not depend from more than one independent claim." In fact, in MPEP §608.01(n), part F, entitled "Handling of Multiple Dependent Claims by the Examiner," there is provided a "Fee calculation example." In that example, there is shown a multiple dependent claim (claim 10) depending from two different independent claims, and this claim is indicated to be a proper one. Even more mystifying to

Applicants is the fact that, even if there were a prohibition against claims depending from more than one independent claim, the claims objected to by the Examiner are not such claims; the only independent claim from which any of the objected-to claims depends is claim 1.

Claims 1, 2, 27, 28, 30 and 32 stand rejected under 35 U.S.C. §102(b) as being anticipated by either U.S. patent No. 4,849,414 to Loots et al. or U.S. Patent No. 5,672,592 to Jackson et al. Applicants disagree with this assessment.

With regard to the Loots patent, the Examiner specifically cites compound RN 118636-20-7. The Examiner sets forth specific moieties in the definitions of some the components of instant generic formula I that allegedly can be found in compound RN 118636-20-7. For one, the Examiner asserts that the cited compound contains a proline isostere (Applicants assume this is what the Examiner meant to say) at the position corresponding to substituent  $R_4$  in the present generic formula.

In the first place, the definition of substituent  $R_4$  in the present application does not encompass a proline isostere. The scope of  $R_4$  in the claims considered by the Examiner in the present Office Action is limited to phosphinate derivatives. Even the scope of  $R_4$  in the claims as originally filed—encompassing not just the phosphinate groups but also hydroxyamide and oxycarbonyl groups—did not include proline

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isosteres. In any event, it can be seen from a comparison of instant formula I and compound RN 118636-20-7 that the proline isostere of the latter must correspond to substituent  $R_3$ , not  $R_4$ , of the former. While the definition of  $R_3$  includes "a carboxylic acid isostere," this would not include a proline isostere either. In any case, this portion of the definition of  $R_3$  has been deleted by amendment herein in the interest of expediting prosecution.

Still further, the Examiner has not mentioned anything about a possible correlation between the component of RN 118636-20-7 that corresponds to substituent  $R_6$  of the present formula and the definition of substituent  $R_6$  in the present claims. In the compound cited by the Examiner, the moiety that corresponds to  $R_6$  of the instant generic formula is that which includes everything appearing to the right of the phosphorus of the phosphinate group (corresponding to  $R_4$  in the instant generic formula). That is to say that the  $R_6$  counterpart is n-butyl-NH-C(O)-CH((CH<sub>2</sub>)<sub>4</sub>-NH<sub>2</sub>)-NH-C(O)-cyclobutane. There is nothing in the definition of instant substituent  $R_6$  that would provide for such a moiety in the presently claimed compounds. For several reasons, then, it cannot be said that compound RN 118636-20-7 is encompassed by the generic formula of instant claim 1.

Similarly, the Examiner's assessment with respect to compound RN 200699-96-3, the compound particularly cited in

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connection with the Jackson patent, is in error. This analysis is even simpler than that for the compound cited in connection with the Loots reference.

In matching up the various components of compound RN 200699-96-3 with the components of the instant generic formula, one sees that the component of the cited compound corresponding to substituent  $R_1$  is an unsubstituted pyridyl moiety. As is clear from the instant claims, when  $R_1$  is pyridyl, i.e., "6-membered aromatic heterocyclyl containing a single heteroatom, which heteroatom is nitrogen," it must be substituted with one or more basic groups. Thus, the generic formula of the present application cannot be said to encompass compound RN 200699-96-3.

Further in connection with this latter compound, Applicants note that the only way that the portion corresponding to instant substituent  $R_6$  could match the definition of  $R_6$  in present claim 1 is if  $R_6$  were substituted. In particular,  $R_6$  would have to be  $C_1$  alkyl substituted by aryl. Thus, the Examiner's analysis for the purpose of leveling a prior art rejection again requires that  $R_6$  be substituted. However, at the same time, the Examiner denies the existence of support for such substitution for the purpose of leveling a §112 rejection. The Examiner cannot have it both ways.

Applicants note that the Loots reference was erroneously listed on the Notice of References Cited as US 4,848,414 to



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**Cahuzac.** It is respectfully requested that the Examiner issue a new Notice with the correct citation to the Loots, et al. patent.

Claim 1 has further been amended herein to more particularly recite the intended scope of the claims with respect to substituent  $R_1$  when it is a heterocyclic moiety, i.e., to segregate said moieties into aromatic and aliphatic heterocycles. Applicants wish to remind the Examiner that these same amendments were previously introduced during prosecution of the copending divisional application, Serial No. 11/293,060, and that the support for the amendments that was cited by the Applicants, as well as the amendments themselves, were accepted by the Examiner in the divisional.

Still further, claim 1 has been amended to restore the original scope of substituent  $R_1$  with respect to alkyl moieties. Early during prosecution of this application, the Examiner cited a prior art reference (that of Usik), and Applicants amended claim 1 to recite that  $R_1$ , when alkyl, is  $C_2-C_6$  alkyl. However, since that time, the scope of the instant claims has been limited further, and there is no conceivable overlap between the scope of the present claims, even with  $R_1$  defined as  $C_1-C_6$  alkyl, and the single compound disclosed in the Usik reference. More particularly, the component of the Usik compound corresponding to instant substituent  $R_4$  is COOH. The limitation of substituent

R<sub>4</sub> during prosecution of the present application has excluded the Usik corresponding substituent and, for that matter, all derivatives thereof. It is respectfully requested, then, that the amendment herein to restore the original scope of the claims with respect to R<sub>1</sub> be entered.

The arguments presented above fully address all of the rejections and objections made by the Examiner. Furthermore, no new matter has been added, or new issues raised, by the amendments made herein. Accordingly, this application is condition for allowance. Reconsideration and allowance of the application with pending claims 1, 2, 27-30 and 32 are respectfully requested. Rejoining and allowance of the withdrawn claims are also respectfully requested. Should any matters require attention prior to allowance, it is requested that the Examiner contact the undersigned.

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No fees should be due in connection with this communication. However, should it be determined that a fee is required for any reason, the Commissioner is hereby authorized to charge it to Deposit Account No. 23-1703.

Dated: July 6, 2007

Respectfully submitted,



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